

REMARKS

Reconsideration of the rejections set forth in the Office action mailed November 12, 2008 is respectfully requested. Claims 1-3, 5-8 and 17-25 are under examination; claims 4 and 10 have been withdrawn from consideration; claims 11-16 have been cancelled; and claim 25 is added with this amendment.

I. Amendments

Applicants have amended claim 1 to delete the phrase “an antimicrobial agent”. Claim 1 has also been amended to recite “an isolated compound” of formula **I**. Support can be found in the specification at, for example, page 9, lines 5-6.

Applicants have added claim 25. Support for claim 25 can be found in original claim 8.

No new matter is added by the amendments.

II. Priority

The Examiner has indicated that the earliest US effective filing date for the instantly claimed subject matter is 6/25/2003, the filing date of provisional application 60/482,630.

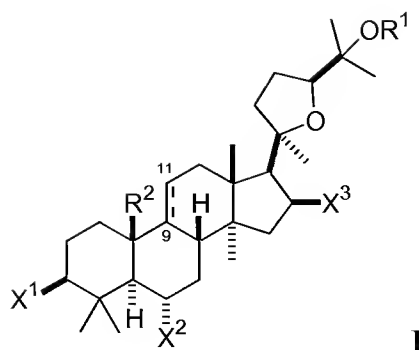
III. Claim Rejections under 35 U.S.C. § 103

Claims 1-3, 5-8, and 17-19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chou (US Pub. No. 2003/0108629, Pub Date July 12, 2003, filed July 16, 2002) in view of the web page at www.drugs.com/npp/astragalus.html (found Oct. 20, 2008). Applicants respectfully traverse the rejection in view of the following remarks.

A. The Claims

Independent claim 1, on which claims 2-3, 5-8, and 17-19 are dependent, is directed to a method for conditioning the skin, comprising:

applying topically to the skin a formulation comprising an isolated compound of formula **I**:



where:

each of X^1 , X^2 , and X^3 is independently selected from hydroxy, lower alkoxy, lower acyloxy, keto, and a glycoside;

OR^1 is selected from hydroxy, lower alkoxy, lower acyloxy, and a glycoside; wherein any of the hydroxyl groups on said glycoside may be substituted with a further glycoside, lower alkyl, or lower acyl, such that the compound includes a maximum of three glycosides; and

R^2 is methyl and ---- represents a double bond between carbons 9 and 11; or, R^2 forms, together with carbon 9, a fused cyclopropyl ring, and ---- represents a single bond between carbons 9 and 11;

and wherein said formulation further comprises an ingredient selected from the group consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant, and an ingredient selected from the group consisting of a preservative and an antioxidant.

B. The Office Action Position

The Office Action states (pages 4-5) that Chou applies *Radix Astragali* root to the skin but does not specifically teach conditioning the skin. Although the Chou reference allegedly suggests the topical use of *Radix Astragali* and herbal fruits, these compounds and their topical application are not immediately envisaged, and therefore the rejection is made under obviousness. It allegedly would have been obvious to employ a topical formulation because the Chou reference suggests such a formulation.

While the Office agrees that the Chou reference does not teach conditioning of the skin, it alleges that one would have had a reasonable expectation of success, in view of the Chou reference, that applying cycloastragenol (sic) to the skin (page 5 of Office Action) would necessarily condition the skin. One allegedly would have been motivated to do so because Chou

suggests the use of *Radix Astragali* to relieve skin infections [140], in combination with herbal fruits such as *Fructus Schisandrac*, which contains anti-microbial/bacterial properties [146], and water and alcohol as a “lubricant” [185]. One allegedly would have been motivated to use water and alcohol as a lubricant.

With respect to dependent claims 23 and 24, the Office Action states (page 6) that the telomerase activity and cell refluence properties recited, while not explicitly disclosed by the prior art reference of Chou, would allegedly be inherent because the function, property and characteristic of the composition taught by Chou is allegedly the same as that of the instant claims.

C. Applicants’ Response

C1. The Cited Art

The cited reference www.drugs.com/npp/astragalus.html (found Oct. 20, 2008) was published after the filing date of the present application and accordingly is not a prior art reference. The Office cannot use this reference in making the rejection.

The cited reference Chou describes compositions including “an aliquot of the herb *Herba Epimedi*” and “an aliquot of at least three supplemental herbs” which are selected from a group of eight herbs, one of which is *Radix Astragali*, or *Astragalus membranaceus* root. The reference teaches that these multi-herb compositions should be administered for “treatment of various kidney disorders or the promotion of kidney health and to the overall health of the kidney”, including “treatment of prostate cancer, prophylactic prostate health, reduction of polyuria, incontinence, proteinuria, as well as for sexual satisfaction” (Abstract).

Firstly, applicants note that, contrary to the Examiner’s statement on page 5 of the Office Action regarding the Chou reference, cycloastragenol is not reported to be a component of *Radix Astragali*. (See e.g. Kitigawa *et al.*, *Chem. Pharm. Bull.* **31**(2):689-697, of record, where cycloastragenol is prepared by hydrolysis of native components of the root.) Moreover, none of the isolated compounds now recited in applicants’ claim 25 are reported to be components of *Radix Astragali*. As described in the applicants’ specification at page 21, line 20 to page 22, line 5, and in the working Examples, these compounds are prepared synthetically.

At paragraph [0140], Chou teaches that *Radix astragali* is indicated for a large variety of disease states; i.e. it purportedly “reinforces vital energy (qi), relieves skin infection, and

promotes tissue regeneration. Invigorates the vital energy (qi) and spleen. For spleen deficiency with poor appetite, loose stool, fatigue and bleeding. For replenishing the collapse of the middle-jiao energy manifested as prolapse of the rectum, hysteroptosis and gastropstosis. Use on common colds in debilitated patients and superficies-asthenia with profuse sweating. Used to treat unruptured abscess, unhealed carbuncle, skin erosion, unhealed wounds, skin rash diseases, and skin infection of the yin type. Recently it has also been used for peptic ulcer and atrophic gastritis.”

Clearly the root has been taught for a wide variety of different and conflicting uses. One skilled in the art would not necessarily have taken from this recitation that any particular isolated component of *Radix astragali* could be used for skin conditioning. Any one of many components of the root could have been responsible for the disclosed effects of *Radix astragali* recited in Chou. (For example, as stated at paragraph [0038] of cited reference Wei, below, *radix astragali* is “rich in polysaccharides and contains glycosides, aponins and essential fatty acids.”)

C2. Analysis

Applicants submit that the Examiner has failed to apply the proper legal standards for comparing the present invention to the cited reference(s). As per M.P.E.P. §2141.02, in “determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious but whether the claimed invention as a whole would have been obvious”. *Statoglex Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983).

The independent claim is directed to a method of skin conditioning, and it requires administering, topically to the skin, a formulation of a specified isolated compound with a first formulation ingredient (emulsifier, surfactant, thickener, skin emollient or lubricant) and a second formulation ingredient (preservative or antioxidant).

The cited reference does not disclose a composition comprising the second formulation ingredient (preservative or antioxidant). In addition, the “9-herb composition” taught by Chou and used for all data collection (see paragraph [0195] and following, including all the Examples) is stated not to contain detectable levels of astragaloside (See Table III in Chou). Finally, although the reference mentions topical application in a standard list of administrative routes

(“oral, rectal, parenteral, intravenous, topical, transdermal, subcutaneous and intramuscular”), there is no teaching of how such administration would be carried out, and it is unlikely that topical application would be feasible for treatment of the kidney or prostate (see Title and Field in Chou), where local or systemic administration would clearly be required.

Furthermore, the biological activity reported in Chou teaches away from the claimed subject matter, which is directed to a method of conditioning the skin. As stated in *In re Geisler*, 116 F.3d 1465, (Fed. Cir. 1997) citing *in re Soni*, 54 F.2d 746, 750 (Fed. Cir. 1995), a prima facie case of obviousness can be rebutted by a showing that the art in any material respect taught away from the claimed invention.

In treatment of prostate cancer as emphasized in Chou, the desired effect is shown to be inhibition of cell growth, the opposite of the biological effect shown by the applicants. See the Examples in Chou, e.g. at paragraphs [0222] (“a 30% reduction in cell growth”; “a significant reduction in cell proliferation”); [0226] (“induction of apoptosis in treated cells”); [0235] (“proliferation of these cells was significantly inhibited”; “85% reduction in cell proliferation”); [0236] (“completely abolishing the colony forming ability of DU-145 cells”); [0241] (“completely abolished focus-forming ability of JCA-1 cells”); and [0244] (“Increasing the concentration of the ethanolic extract resulted in a greater than 95% reduction in cell proliferation”). One skilled in the art, given this disclosure, would not consider that the compositions in Chou would be useful for skin conditioning.

The biological activity touted by the reference, as noted above, is in direct contrast to the benefits obtained by the subject compounds of the applicants’ claims, as taught by the applicants in the instant application. “It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art....A reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered.” *Bausch & Lomb v. Barnes-Hind/Hydrocurve* (796 F.2d 443, 230 USPQ 416, Fed. Cir. 1986) A skilled person looking for a method of skin conditioning would not look to a reference focused on inhibiting cell growth for treatment of prostate cancer.

With respect to dependent claims 23 and 24, the Office Action states that the telomerase activity and cell refluence properties of instant claims 23 and 24 are not explicitly disclosed by Chou but would be inherent because of the function property and characteristic of the composition taught by Chou. If the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are allegedly necessarily present.

This part of the rejection is traversed for the following reasons. A claim limitation is inherent in the prior art if it is necessarily present in the prior art, not merely probably or possibly present. *Akamai Technologies v. Cable & Wireless Internet Services, Inc* 344 F.3d 1186, 68 USPQ 2d 1186.

In this case, as indicated above, the Chou composition showed inhibition of cell growth and in some cases cell apoptosis. Accordingly, the composition of Chou does not necessarily produce a telomerase activity at least 25% greater than observed in a vehicle control. Further, the 9-herb composition of Chou does not necessarily produce an amount of cell refluence in a scratch assay of keratinocytes which is at least 25% greater than that seen in untreated or other controls.

For these reasons, withdrawal of this rejection under 35 U.S.C. 103(a) is respectfully requested.

IV. Further Rejections under 35 U.S.C. § 103

Claims 20-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chou (US Pub. No. 2003/0108629) in view of www.drugs.com/npp/astragalus.html (found Oct. 20, 2008) as applied to claim 1 above, and further in view of Wei *et al.* (U.S. Pub. No. 20020164387; Pub Date Nov. 7, 2002).

Chou allegedly teaches a composition that comprises *Radix astragali* to help promote healing of damaged tissues. The Office Action states that it allegedly would have been obvious at the time of the invention to have added an oil to the composition because Wei *et al.* teaches that oils may be used for texture or shelf-life enhancement.

This rejection is traversed for the following reasons. The cited references Chou and www.drugs.com/npp/astragalus.html (the latter of which is not available as prior art) are addressed above.

Wei *et al.* teaches an oral herbal composition “comprising rhubarb, red saga root, astragalus, turmeric, and dried ginger and various combinations thereof” for reducing weight gain and effecting weight loss (Abstract). At paragraph [0038], Wei states that *Radix astragali* is rich in polysaccharides and contains glycosides, aponins and essential fatty acids. Wei states that the root has a variety of therapeutic activities, including healing of damaged tissues, protecting the liver against chemical damage [0036], increasing production and activity of white blood cells, easing chemotherapy and radiation side effects, inhibiting the spread of tumors [0037], preventing clotting and coronary heart disease, lowering blood pressure, facilitating digestion, increasing metabolism, and controlling diarrhea [0038].

Wei does not teach topical administration of the herbal composition or the use of the herbal composition for skin conditioning. The passage cited by the Office Action in support of the use of oil is found in a discussion of oral liquid preparations [0011]. There is no discussion of the use of oil in a topical formulation.

Accordingly, Wei *et al.* does not cure the deficiencies of the Chou reference. Withdrawal of this rejection is respectfully requested.

V. Conclusion

In view of the foregoing, the applicant submits that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

Respectfully submitted,

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Date: February 12, 2009

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